GLOBAL CLIMATE CHANGE AND HEALTH: DEVELOPING A RESEARCH AGENDA FOR THE NIH

JOSHUA P. ROSENTHAL, Ph.D., and CHRISTINE M. JESSUP, Ph.D.
(*both by invitation*)

BETHESDA, MARYLAND

ABSTRACT

Global climate change is receiving worldwide attention because of its anticipated impacts on the Earth's physical and biological systems. Through its effects on natural and human environments, climate change will likely impact economic viability and human health and well-being. The impact of climate change on human health is likely to be complex and significant, including effects on cancers, cardiovascular and respiratory disease, food-, water-, and vector-borne diseases, heat-related illness, mental and social well-being, nutrition, trauma, and vulnerable demographic sectors. Most assessments predict that these effects will disproportionately affect the poor, the elderly and the young, especially those living in Africa and Southeast Asia, where environmental conditions are poor, health infrastructure is weak and the burden of disease is great. Enormous efforts are underway to plan and finance climate change adaptation programs within national governments (including multiple U.S. agencies), United Nations organizations and private philanthropies. However, these endeavors are proceeding with a relatively poor understanding of the nature and magnitude of probable effects of climate change on health. The National Institutes of Health (NIH) already funds a portfolio of projects that are indirectly related to the concerns posed by global climate change. At the NIH, we have recently established an agency-wide planning group to assess the research questions in health and medicine that climate change presents, to link this agenda to parallel activities across other agencies of the U.S. Government (USG), and to advance a NIH research agenda in this area.

The 2007 Report of the Intergovernmental Panel on Climate Change [1] synthesized models of climate change that depend on large-scale atmospheric dynamics and emission scenarios. The atmospheric events most relevant to human health include changes in mean

Correspondence and reprint requests: Joshua P. Rosenthal, Ph.D, Division of International Training and Research, Fogarty International Center, National Institutes of Health, Bethesda, Maryland 20892-2220, Tel: 301-496-1653, Fax: 301-402-0779, E-mail: joshua_rosenthal@nih.gov.

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conditions and variability of temperature, precipitation, humidity and wind that are likely to 1) alter the intensity and geographical distribution of extreme weather events, including heat waves, hurricanes, floods, droughts and forest fires, 2) significantly raise water levels in coastal regions, 3) alter distribution of vector insects and mammals, 4) exacerbate health-relevant air pollution, including particulate matter and pollen, 5) intensify the existing burden of malnutrition, and 6) increase human exposure to xenobiotic toxicants due to the deterioration of the natural and man-made environments. Some of these pathways and some general health-related adaptation measures are illustrated in Figure 1. Recently, the *American Journal of Preventive Medicine* devoted a special issue to the topic of climate change. Titled "Climate Change and the Health of the Public", this issue contains 16 articles on many of these health impacts of climate change, as well as adaptation strategies that can foster resilience in the face of climate change (summarized in [2, 3]).

In general, the effects of climate change are expected to emerge gradually over the next 5 to 50 years, but in many cases a biological signal can already be seen. For example, between 1994 and 2002 the length of the allergenic pollen season in Montreal has increased from approximately 40 days to almost 70 days per year, although it should be noted that multiple influences are likely to have caused this change [4]. The effects of an extended vegetation growing season and increased atmospheric CO_2 on pollen production and their implications for aller-

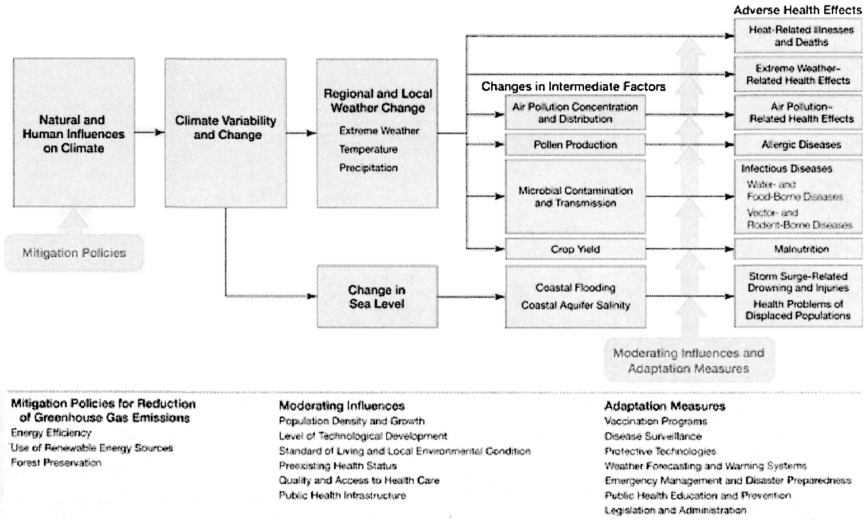

FIG. 1. Potential health effects of climate change. (Reproduced from [30])

gic reactions remain poorly understood. More abrupt and dramatic effects of climate change are also hypothesized and potentially include sea level rise due to both thermal expansion and melting of glaciers, sea ice and ice caps, as well as threshold sea temperature effects that may produce directional changes in ocean currents and rapid climate changes around the world, with associated effects on the severity and frequency of hurricanes, droughts, flooding events, fires and heat waves [5].

Probable Health Effects of Global Climate Change

Health effects are likely to be diverse and significant. Droughts and floods reduce the availability of freshwater and can produce catastrophic sanitation problems and chemical exposures such as those seen with Hurricane Katrina in 2005, as well as long-term toxicity and carcinogenicity due to mobilized chemicals in agricultural soils and drinking waters. Increases in waterborne diseases are likely to emerge [6], both from floods that overwhelm sanitation systems and droughts that force populations to use marginal water sources for drinking.

Studies of interannual variability (i.e. processes that occur on longer timescales than seasonal variability) of temperature and rainfall associated with the El Niño Southern Oscillation (ENSO) have revealed fairly predictable changes in a waterborne disease, cholera [7, 8], and a vectorborne disease, Rift Valley Fever [9, 10], which are likely related to the complex ecological dynamics of the associated organisms. How these disease dynamics may be impacted by long-term directional climate change is unclear; however, studies of the association between ENSO and human diseases provide a framework for understanding how shifts in disease burden are associated with weather and climate.

Climate change models predict that extreme heat events, or heat waves, will become more frequent and intense, and such events will have a major impact on areas that are not well adapted to them [11]. Increased mortality is a common feature of heat waves, particularly among the elderly. Many of these deaths are related to cardiovascular, cerebrovascular and respiratory causes, and may be exacerbated in urban environments due to the urban heat island effect. The 1995 heat wave in Chicago resulted in excess heat-related hospitalizations due to dehydration, heat stress and heat stroke [12]. Basic research on the health effects of ambient temperature changes is needed. In general, researchers are only beginning to understand the influence of climate on air pollution [13]. Furthermore, the effect of ambient temperature on human susceptibility to air and water pollution is poorly understood.

Extreme weather events such as heat waves, hurricanes, droughts and floods projected by climate change models also take a toll on mental health. Although not related to climate change, following the December 26, 2004 tsunami disaster, 14–39% of children in coastal communities in Sri Lanka suffered from posttraumatic stress disorder [14]. Extreme weather events associated with climate change may have similar impacts.

Ultraviolet (UV) radiation has long been linked to skin cancers and cataracts. Although ozone depletion and associated increases in UV exposure are generally considered to be separate from global warming, a recent report by the World Health Organization highlights that global warming may interact with stratospheric ozone depletion, resulting in increased UV exposure [15]. Furthermore, human behavior changes associated with climate change may increase exposure to UV and risk of associated diseases [16].

The effects of climate change are likely to differ both within and between continents and to have complex interactions with existing health burdens, health protection and delivery systems. The impacts on health in the United States are likely to be significant, particularly for more vulnerable subpopulations such as children because of their developing physiology [17], and the elderly due to their susceptibility to respiratory and cardiovascular diseases [18, 19]. The impacts are likely to be even greater in developing countries. For example, some regions of Africa will experience more frequent and more severe droughts; many small island states could experience increased flooding [20]. The displacement of populations due to droughts or flooding and the resulting human migration are likely to strain existing health infrastructures, exacerbating the health impacts of climate change. Changes in infectious disease dynamics and UV radiation exposure will differ across altitudinal and latitudinal gradients, and susceptibility will vary with genetic and behavioral factors that differ around the world. Climate change, through its non-uniform distribution of health impacts, presents a significant challenge to global health [21].

Finally, the potentially significant health effects of climate change mitigation strategies (e.g., global shifts in energy production and use that are intended to mitigate CO_2 production) cannot be ignored. For example, the use of dams to generate hydroelectric power will affect the distribution and intensity of vectorborne diseases [22] and may displace populations, yielding the health problems that often accompany human migration [23]. Land-use changes associated with the increased demand for biofuels may have unanticipated health consequences, and the impact of biofuel exhaust on human health requires

further research [24]. Some of these health effects as well as some of the interventions effective in mitigating and adapting to climate change are highlighted in Figure 1.

Current NIH Climate change relevant research

Because of the complexity of climate change and its relationship to traditional health research, it has been difficult to develop an accurate assessment of the relevant research portfolio. The National Eye Institute, the National Cancer Institute (NCI), the National Institute of Arthritis and Musculoskeletal and Skin Disease, and the National Institute of Environmental Health Sciences (NIEHS) are currently partners in the U.S. Global Climate Change Research Program. This program has principally been tasked with reporting relevant science activities across the USG. To automate and standardize the classification of grants into specific disease categories in order to improve the consistency of budget reporting to the Congress and the public, the NIH has recently developed the Research, Condition and Disease Classification (RCDC) Project. Using this automated text-mining system, we examined the extent to which the NIH is already engaged in research relevant to the health effects of climate change. We completed a preliminary analysis of the grants that the NIH RCDC process categorized. If we look across the entire NIH portfolio, using the current family of Climate Change Fingerprints developed by the RCDC, the agency funded 576 climate change related projects in 2006. Figure 2 illustrates our categorization of the 2006 portfolio by study type, health effect focus, study objective and climate or ecological variable. A brief analysis of the 2006 project follows.

1) Many NIH Institutes and Centers (ICs) fund research categorized under climate change according to the RCDC process (Table 1). The largest portfolios of climate change-related research in 2006 were funded through the NCI and the NIEHS. NCI-funded projects primarily addressed the effects of exposure to UV radiation and carcinogens. NIEHS-funded projects focused on the health impacts of air pollution and water pollution.
2) According to this analysis, NIH-funded projects examined many different health impacts (cancer, cardiovascular disease, infectious disease, respiratory diseases, malnutrition, mental health and trauma, neurological health, reproductive health, and vision) in relation to a variety of environmental impacts (air and water pollution, extreme weather such as fires and flooding, heat stress, ozone depletion/UV radiation).

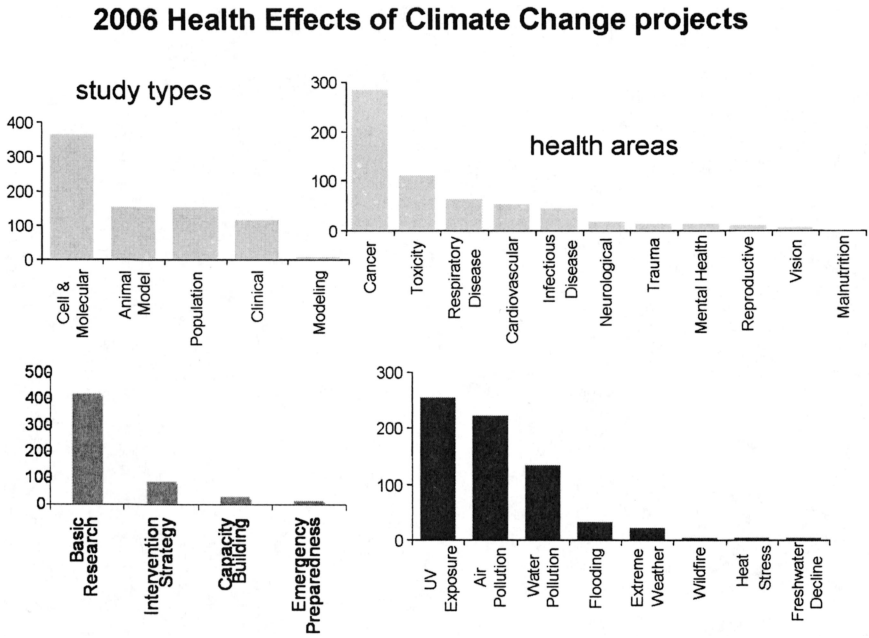

FIG. 2. Categorization of 2006 NIH projects indentified as related to Health Effects of Climate Change by the NIH RCDC fingerprinting system. Categories are not mutually exclusive.

3) Although many NIH-funded projects were indirectly related to climate change, few projects explicitly referred to climate change or attempted to project its effects. In general, the handful of projects that did refer to climate change focused on infectious diseases and the impact of climate change on pathogen transmission dynamics.
4) According to this analysis, the majority of climate change-related projects funded in 2006 addressed air and water pollution and its effect on cardiovascular disease, respiratory disease, cancer and general toxicity. The projects were overwhelmingly molecular and cellular in nature, with some animal and human studies. The NIH also funded a small number of relevant research projects in populations that may be disproportionately affected by climate change - e.g., studies in developing countries and research on children and the elderly.

Some examples of funded projects are highlighted below.

- The National Institute of Allergy and Infectious Diseases funded research investigating the impacts of climate change on transmission of avian influenza in wild birds.

TABLE 1
NIH Institutes that funded climate change related projects in FY 2006 (in alphabetical order).

Fogarty International Center
National Cancer Institute
National Center for Complementary and Alternative Medicine
National Center for Research Resources
National Eye Institute
National Heart Lung and Blood Institute
National Institute of Allergy and Infectious Disease
National Institute of Child Health and Human Development
National Institute of Deafness and other Communication Disorders
National Institute of Dental and Craniofacial Research
National Institute of Diabetes and Digestive and Kidney Diseases
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Institute of Mental Health
National Institute of Neurological Disorders and Stroke
National Institute on Aging
National Institute on Arthritis and Musculoskeletal and Skin Diseases
National Institute on Drug Abuse
National Library of Medicine

- The National Institute of Environmental Health Sciences supported a study of the environmental factors that influence the production of algal toxins in the marine environment. Under certain environmental conditions, harmful algal blooms produce potent toxins that can cause human illness and mortality.
- The National Library of Medicine funded a study of historical records of the 1900 bubonic plague outbreak in San Francisco with the goal of informing contemporary management of public health campaigns for epidemics and disasters.
- One project in the portfolio of the National Institute of Child Health and Development is investigating the impacts of natural disasters on mortality, family disruption, physical and mental health, and economic resources. Another project examined the effects of prenatal exposure to polychlorinated biphenyls (PCBs) and methylmercury in populations with different exposure levels to elucidate the impacts of these compounds on central nervous system development and to explore intervention strategies.
- The National Center for Research Resources funded a research center that is studying the impacts of ozone exposure on lung development using a primate model.
- The National Heart, Lung, and Blood Institute funded a cohort study that looks at the impact of air pollution on asthma in children with the goal of identifying risk factors and guiding prevention strategies.
- The Fogarty International Center funded a project that is investi-

gating transmission of leptospirosis, a zoonotic disease, from its natural reservoir to human hosts and how these dynamics might be affected by climate change and land use changes.

Using a revised fingerprint, the FY 2008 project list has recently been released (January 2009). The number of projects categorized under Health Effects of Climate Change is significantly larger (820 projects). A full analysis of this more recent project list remains to be completed. This is a priority activity for the Trans-NIH Working Group on Climate Change and Health (described below).

Research Needs to Address Health Effects of Climate Change

The Intergovernmental Panel on Climate Change (IPCC) Fourth Assessment Report identified a number of key uncertainties and research needs to support efforts to adapt to climate change (1). These include: a) development of methods to quantify the current impacts of climate and weather on a range of health outcomes, particularly in low- and middle-income countries; b) development of health-impacts models for projecting climate change-related impacts under different climate and socio-economic scenarios; c) investigations on the costs of the projected health impacts of climate change; d) the effectiveness of adaptation efforts; and e) understanding the limiting forces, major drivers and costs of adaptation.

The U.S. Climate Change Science Program's (CCSP) recent assessment of health effects (25) also includes a set of NIH-relevant research and capacity building recommendations. These are summarized as follows: a) improve characterization of exposure-response relationships, particularly at the regional level; b) evaluate the early effects of changing weather patterns on climate-sensitive health variables; c) develop quantitative models of possible health impacts of climate change; d) increase our understanding of the processes of adaptation, including social and behavioral aspects; e) evaluate the implementation of adaptation measures; and f) improve estimates of "co-benefits" of adaptation and mitigation efforts.

The World Health Organization and the U.S. Institute of Medicine of the National Academies are both poised to issue their own reports and recommendations on research needs. These research needs are driven in part by the needs of policy-makers for quantitative, integrated and targeted population-level assessments of priority health risks. Such quantitative information is critical to inform public health and medical planning that is already underway by the Centers for Disease Control and other agencies, and to strategically guide the hundreds of millions

of dollars of development aid already beginning to funnel its way through the World Bank, the United Nations Framework Convention on Climate Change, national governments, and foundations.

Some of these 'risk assessment' needs may be addressed by the NIH. However, it is also evident that the needs outlined by these science policy organizations point to a broad agenda that includes basic, clinical, translational and implementation science areas for which the NIH has some unique and relevant capabilities. Basic exposure-response studies at individual and population levels are needed for a range of climate-related phenomena. For example, how much of the global rise in asthma is attributable to the effects of climate change on particulate matter exposure versus other factors, such as changes in immune status ([26])? Answering such fundamental questions requires the work of molecular biologists, clinicians and epidemiologists. For another example, consider the effects of climate change on infectious diseases. The IPCC assessment projects "with high confidence" that climate change will have mixed effects on malaria, one of the world's biggest killers. In some places, the geographical range of malaria vectors will contract; in other areas the geographic range will expand, and the transmission season may change ([1]). However, there is debate within the vector-borne disease research community as to how influential these shifts will be relative to other factors such as drug resistance and changes in health services, and whether significant changes will occur within the next five years or over 20 years ([27–29]). To address this question, physiological, demographic, ecological, and social/behavioral studies and health systems analyses are necessary. Development of new analytical and predictive tools, intervention methods, as well as evaluation of existing health projects and programs may be needed and would require NIH research and investments.

A Trans-NIH Climate Change and Health Working Group has been formed to assess the research needs and opportunities *vis-à-vis* our current climate change-relevant portfolio. Over the coming months, the NIH Working Group will assess whether the current NIH portfolio, characterized as climate change-relevant by the automated RCDC process, is well matched to these recommendations. The RCDC categorization of NIH grants is evolving, as is our interpretation of research on the health effects of climate change. However, a preliminary analysis of the portfolio in relation to these objectives suggests that there are some significant gaps. We will analyze these explicitly in the coming months. What is clear at this point is that involvement and contributions by physician-scientists will be particularly valuable in the development and evaluation of clinical and public health strategies

to minimize the impacts of climate change on health. We would welcome focused consideration by the American Clinical and Climatological Association in this area.

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SYMPOSIUM DISCUSSION

Hochberg, Baltimore: So Dr. Lindberg, in your review of the previous transactions and the focus on altitude and sunlight, that raises the issues of vitamin D and the effects of vitamin D on health, both in terms of its relationship to bone disease but more so on the relationship on immune function, and then maybe that could feed into some comments from the speakers who have mentioned increases in ultraviolet radiation, which could affect production of vitamin D, and then the effects that vitamin D might have both with regard to prevention of some infectious diseases, as well because of its effect on the immune system.

Lindberg, Bethesda: I find myself unable to comment on that.

Billings, Baton Rouge: In one of the most recent New England Journals of Medicine, one of the cardiologists had as a conflict of interest the fact the he was supported

by seven drug companies. I am proud to say, and embarrassingly, I don't have any conflicts of interest because I don't have any support, but my comment is that in the days of the early climatologists, how pure were we? The railroads supported our efforts, the communities, as you alluded to, had a cottage industry in Saranac Lake. How pure were we with our earlier roots?

Lindberg, Bethesda: I wondered exactly that. I guess it would take a little bit more time than I had to give it to go down to the real details, but I emerged with a kind of an admiration for these people who, as I said, were fascinated by all of these atmospheric measurements; but I think, in the end, the best of them had in mind that there were natural laws that they perhaps could come to understand, but I think it's probably true that whether you owned a sanitarium might influence your admiration for the salubrious nature of the climate. I guess I would have to look further, but it wouldn't be a task that I would enjoy. So I might put it off.

Goldfinger, Boston: Dr. Lindberg, in your extensive, thoughtful presentation and particularly your review of our past annals and archives, I wondered if you came across anything with respect to the salinity of the air. I was thinking of this, having visited the UNESCO site of the salt mine, and that's out of Krakow, and was told that pulmonologists brought their patients with respiratory insufficiency into the depths of this mine for the therapeutic quality of the air that they would be breathing.

Lindberg, Bethesda: I have heard that too, but I guess I just don't know enough about that. It's hard to imagine that there would be, but people have talked about the glories of the air in their local towns since back to the ancient Greeks. So maybe it is in the eye of the beholder.

Sacher, Cincinnati: One thing that hasn't been mentioned is the impact of all these vectors on the blood supply and blood donation, for example, Chagas disease. You know donors are excluded from going to malarial areas or areas with West Nile Virus and that sort of thing as well. So I wonder if our speakers can comment on that. It is a major issue because, actually, you also realize that in terms of blood donors, it was initially felt that two-thirds of the population could donate. We now know that it is only about 30%, and only 5% do, and of course, there is an increasing use of blood transfusions currently with all the various chemotherapies that we use.

Lindberg, Bethesda: I was talking with people from Africa just last week, and they confessed that they weren't even testing for malaria—simply using the blood draw. So that's asking for a whole lot of trouble. We even test of course for hepatitis virus and should. Josh, were you going to comment?

Rosenthal, NIH: The Chagas story, to the best I understand it, has more to do with immigration patterns, rather than movement of disease vectors. However, it is highly unlikely that vectors such as those won't be effective. It just hasn't been well studied. Similarly with West Nile, but malaria is a case where, of course, it is a blood supply issue, and you would expect that to be affected by climate.

Lindberg, Bethesda: To me, this proposition of study of climate and its effect on health actually butts right up against another major problem or challenge for us, namely disaster information management, which we also don't do terribly well, in floods and hurricanes and so forth, and challenge us. I think in both of those respects, the answer is local knowledge. In other words, you have to bail out the local area, and we have all seen that in spite of Homeland Security and FEMA and everything else it is hard to feel more safe. You know, I don't feel more safe. So we are looking at that particular matter, partly because I haven't asked anybody for a squadron of helicopters, but on the other hand, I think the biomedical people, particularly the communications and library types, can certainly not do any worse than the failures in communication we have already seen with these natural disasters and the man-made ones as well. So it seems to me that we

are being forced to deal with these bigger issues that we have been able to, if not sweep under the rug, but turn our heads away from, and I think there is science to be done in there; but I think the first step is to look to our local areas and be sure that we understand how it will work out for our hospitals and our populations. I remember, well it was sort of shocking, but I won't ever forget it, a briefing that AAMC gave shortly after Katrina; and CEOs of the three major medical centers in New Orleans giving us their wisdom at a 7 a.m. briefing, and the one director said that so far as he was concerned, the two things that you had to have in order to run a hospital were a force of armed guards and diesel generators. I was so amazed to hear a hospital administrator talk that way, but he then proceeded to describe that you know the institution had to make a decision: are you going to run a hospital or a refuge? And you know even if you have your staff organized into team A and team B and they've got badges and stuff, you know you've got to keep the others out; and having the power supply in the basement, in the case of a flood you automatically are out of business. So there are all of those considerations that to me were sort of foreign to any training I've ever had and probably foreign to most of the training you've had, but are sort of upon us even so. So I sort of categorize the climate in that same area, but I do think that this Association is the only medical society, perhaps in the world, certainly in the U.S., that is in a position to claim a special interest and expertise in atmosphere and climate, and I think we ought to step up to the bat. In any case, I thank you for your attention.